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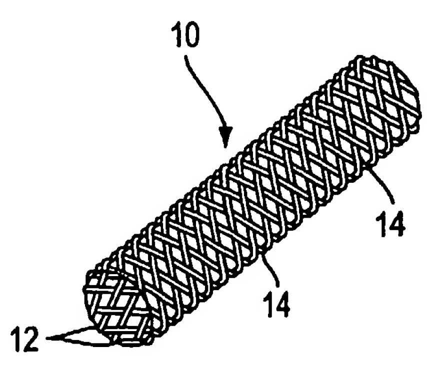
(54) Title: DISINTEGRATING STENT AND METHOD OF MAKING SAME



(57) Abstract: A temporary stent endoprosthesis (10) that does not require an interventional procedure for removal. The disintegrating stent is preferably made from a bioabsorbable polymer, such as by braiding polymer monofilaments into a tubular mesh shape, and the polymer has fracture initiation sites within it that promotes the disintegration of the stent into small pieces that are harmlessly transported out of the body by the vessel contents. Fracture initiation sites may be created by controlling the heterogenous structure of amorphous and crystalline regions, by introducing internal or surface fracture initiation sites, or use of multiple strands with small section size.

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Disintegrating Stent and Method of Making Same

Background of the Invention

1. Field of the Invention

The present invention relates generally to implantable temporary medical prostheses that do not require interventional procedures for removal. In particular, the present invention is a disintegrating implantable medical prosthesis that disintegrates into small pieces that are harmlessly transported out of the body by normal body function.

2. Related Technology

Medical prostheses frequently referred to as stents are well known and commercially available. They are, for example, disclosed generally in the Wallsten U.S. Patent 4,655,771, the Wallsten et al. U.S. Patent 5,061,275 and in Hachtmann et al., U.S. Patent No. 5,645,559. Devices are used within body vessels of humans for a variety of medical applications. Examples include intravascular stents for treating stenoses, stents for maintaining openings in the urinary, biliary, tracheobronchial, esophageal, and renal tracts, and vena cava filters.

A delivery device which retains the stent in its compressed state is used to deliver the stent to a treatment site through vessels in the body. The flexible nature and reduced radius of the compressed stent enables it to be delivered through relatively small and curved vessels. In percutaneous transluminal angioplasty, an implantable endoprosthesis is introduced through a small percutaneous puncture site, airway, or port and is passed through various body vessels to the treatment site. In endoscopy, the delivery device is passed through the instrument channel of the scope. After the stent is positioned at the treatment site, the delivery device is actuated to release the stent. Following release of the stent, the stent is allowed to self-expand within the body vessel, in the case of self-expanding stents, or alternatively, a balloon is used to expand the stent. The delivery device is then detached from the stent and removed from the patient. The stent remains in the vessel at the treatment site as an implant.

Stents must exhibit a relatively high degree of biocompatibility since they are implanted in the body. An endoprosthesis may be delivered into a body lumen on or within a surgical delivery system such as delivery devices shown in U.S. Patent Nos.

4,954,126 and 5,026,377. Suitable materials for use with such delivery devices are described in U.S. Patent Application Serial No.08/833,639, filed April 18, 1997.

Commonly used materials for known stent filaments include Elgiloy® and Phynox® metal spring alloys. Other metallic materials that can be used for stent filaments are 316 stainless steel, MP35N alloy, and superelastic Nitinol nickel-titanium. Another stent, available from Schneider (USA) Inc. of Minneapolis, Minnesota, has a radiopaque clad composite structure such as shown in U.S. Patent No. 5,630,840 to Mayer. Stents can also be made of a Titanium alloy as described in United States Patent No. 5,888,201.

Bioabsorbable stents have also been proposed, for example in U.S. Patent Application serial no. 08/904,467 entitled Bioabsorbable Self-Expanding Stent, filed August 1, 1997, and commonly assigned to the assignee of this application. Such bioabsorbable stents may be formed, for example, from a number of resilient filaments which are helically wound and interwoven in a braided configuration. Such stents assume a substantially tubular form in their unloaded or expanded state when they are not subjected to external forces. When subjected to inwardly directed radial forces, the bioabsorbable stents are forced into a reduced-radius and extended-length loaded or compressed state. Bioabsorbable stents are generally characterized by a longitudinal shortening upon radial expansion.

Bioabsorbable implantable endoprostheses such as stents, stent-grafts, grafts, filters, occlusive devices, and valves may be made of poly(alpha-hydroxy acid) such as poly-L-lactide (PLLA), poly-D-lactide (PDLA), polyglycolide (PGA), polydioxanone, polycaprolactone, polygluconate, polylactic acid-polyethylene oxide copolymers, modified cellulose, collagen, poly(hydroxybutyrate), polyanhydride, polyphosphoester, poly(amino acids), or related copolymers materials, each of which have a characteristic degradation rate in the body. For example, PGA and polydioxanone are relatively fast-bioabsorbing materials (weeks to months) and PLA and polycaprolactone are a relatively slow-bioabsorbing material (months to years).

The implantation of an intraluminal stent generally causes a generally reduced amount of acute and chronic trauma to the luminal wall while performing its function. Stents that apply a gentle radial force against the wall and that are compliant and flexible with lumen movements are generally used in diseased, weakened, or brittle lumens. Such

stents are generally capable of withstanding radially occlusive pressure from tumors, plaque, and luminal recoil and remodeling.

There remains a continuing need for stents with particular characteristics for use in various medical indications. Stents are needed for implantation in an ever growing list of vessels in the body. Different physiological environments are encountered and it is recognized that there is no universally acceptable set of stent characteristics. A surgical implant such as a stent endoprosthesis must be made of a non-toxic, biocompatible material in order to minimize the foreign-body response of the host tissue. The implant must also have sufficient structural strength, biostability, size, and durability to withstand the conditions and confinement in a body lumen.

All documents cited herein are incorporated herein by reference in their entireties for all purposes.

Summary of the Invention

The therapeutic advantage of permanent metal stent implants may be lost after several years of implant residence time in the body. For example, stent occlusion may occur due to collapse of the stent, restenosis from chronic tissue hyperplasia, or plugging from the flow disturbances contributing to biofilm formation or thrombosis. Solid plastic tubular removable stents require an interventional procedure for removal, and dilators typically have to be used repeatedly in periodic interventions to be effective. The disadvantages of permanent metal expandable or solid plastic tubular removable stents are addressed in part by bioabsorbable stents, but bioabsorbable stents can have their own disadvantages.

Fast-absorbing bioabsorbable stents used as short-term implants necessarily release degradation products at a relatively rapid rate compared to slow-absorbing polymers for longer-term stents. The "burst" of degradation products from fast-absorbing stents can potentially cause significant inflammation and hyperplasia leading to obstruction or clinical complications. Slow-absorbing bioabsorbable stents may have acceptable tissue response during absorption, but these stents are present in the body for at least 12 months. In both the cases of fast- and slow-absorbing stents, the implants can break apart into large pieces at locations of high stress or strain when degradation occurs. Such large pieces can cause tissue damage, if the fracture surfaces are sharp, and may lead to luminal obstruction. Prostatic and esophageal stents of this type have had to have

larger pieces removed. There are no temporary stents that do not require an invasive procedure for removal available on the market that behave like the expandable, long-term stents and that can be used as a bridge to adjuvant therapies.

Accordingly, there is provided according to the present invention disintegrating stents for use in a body lumen that are appropriate for short (up to six weeks), medium (from six weeks to six months) and long-term (over six months) implant residence time and that require no interventional procedure for removal. More specifically, the present invention relates to improved stents designed to undergo controlled, purposeful, and beneficial fracture and/or disintegration without the need for interventional removal, in the case of metal or other other biostable materials, or, in the case of bioabsorbable materials, prior to complete absorption or encapsulation of the stent within the vessel wall.

The invention also relates to mechanisms to promote fracture of the stent into small pieces or particles. In particular, the disintegrating stents of the present invention include mechanisms to cause the stents to break apart into small, soft pieces once they are no longer needed. The products of the disintegration of the stent are then harmlessly transported by vessel contents, for example, bile, urine, fecal matter, gastric contents, mucous and air, and eliminated by excretion or exhalation.

The disintegrating stent of the present invention is preferably made of the Wallstent design technology using bioabsorbable polymer monofilaments as described in U.S. Patent Application no. 08/904,467, filed August 1, 1997, the specification of which is incorporated herein by reference in its entirety. Stent designs other than the Wallstent braided construction may also be used according to the present invention, such as a single helical coil, rolled film or sheet, knitted or woven filaments, or extruded tubes. The preferred materials are bioabsorbable polymers, because if some of the disintegration particles become entrapped in the body, they can safely undergo the full absorption process. Bioabsorbable polymer resins such as PLA, PLLA, PDLA, PGA and other bioabsorbable polymers are commercially available from several sources including PURAC America, Inc. of Lincolnshire, Illinois.

While all bioabsorbable stents "disintegrate" during the absorption process, one object of the present invention is to purposely design the implant to cause fracture and/or disintegration to happen, preferably at specific sites and the pieces eliminated from the

body, rather than rely on complete bioabsorbtion of the stent within the body. In particular, the invention relates to engineered biodegradation to promote predictable and designed fracture and/or disintegration of the stent so that small stent pieces may be transported out of the body, rather than relying on the full bioabsorbability of the material to allow complete dissolution of the stent.

While bioabsorbable materials are preferred according to the invention, it is envisioned that other materials, such as biostable polymers and metals may be used according to the invention whereby such stents weaken and fracture into fragments as a result of interaction with naturally occurring body chemicals with assistance from mechanical initiation sites.

The present invention may also be used to cause planned failure of solid plastic tubular biliary stents and other prosthetic surgical implants to make them temporary and self removing.

Methods of engineering planned stent disintegration and/or failure according to the present invention may include but are not limited to: controlling the formation of heterogeneous structure of amorphous and crystalline regions within the stent or stent filaments, creating multiple internal or surface fracture initiation sites, creating localized pre-degraded material, or using multiple strands with small section size to construct the stent. According to the invention, stent disintegration would occur at the initiation sites and the small particles would be transported by urine, bile, fecal matter, gastric contents, or air through the vessels to be excreted or exhaled from the body. Radiopaque agents could be mixed in with the polymer to add radiopacity to the stent.

The present invention also relates to manipulation of the molecular structure of a polycrystalline polymer and/or design of the material of an implant to purposely disintegrate such that the disintegration products become mobile in the vessel system and harmlessly pass out of the body prior to full-onset of the mass degradation process. Polycrystalline bioabsorbable polymers are known to have amorphous regions and crystalline regions. These polycrystalline bioabsorbable polymers are known to degrade preferentially in the amorphous regions first and then subsequently in the crystalline regions.

The conventional objective of materials and implant design engineers has been to control or manipulate the manufacturing process to avoid early disintegration from

fast-degrading amorphous regions by trying to increase the crystallinity of the polymer. The result is that bioabsorbable stents of the prior art are comprised of polymer monofilaments that are generally 40% - 60% crystalline. By contrast, the present invention relates to thermomechanically processing a bioabsorbable polymer to produce *more* fast-degrading amorphous regions in the material to create predictable and/or more numerous sites of polymer fragmentation. Amorphous regions may be created by fast cooling of melt-spun polymer extrudate to prevent nucleation and growth of significant crystalline regions.

The concentration and morphology of the fast-degrading amorphous regions and the mechanical stresses and strains in the implant determine the disintegration product size. According to the invention, the polymer material preferably comprises greater than 60% amorphous regions, or, stated another way, less than 40% crystallized regions. On the other hand, if the amorphous regions comprise too great a proportion of the polymer material, the strength of the monofilament may not be sufficient to survive the braiding process. Accordingly, the amorphous regions preferably do not comprise more than about 80% amorphous regions, or not less than about 20% crystallized regions. Hence, the amorphous regions preferably comprise about 60% to about 80% amorphous regions (corresponding to about 20% to about 40% crystallized regions) and more preferably, the amorphous regions may comprise between about 60% to about 70% (about 30% to about 40% crystallized regions). For some applications which have lower strength requirements for the stent, the amorphous regions may comprise from about 70% to about 80% of the polymer material (corresponding to about 20% to about 30% crystallized regions). The relative proportion of amorphous to crystallized regions may be determined by differential scanning calorimetry.

The degradation rate or manufactured physical and mechanical properties of the slow-degrading or more biostable regions, respectively, determine the physical and mechanical properties of the disintegration products. Preferably, the stents of the present invention are engineered so that the disintegration products are on the order of about 10 microns to one centimeter in size, preferably from about .1 mm to about 5 mm in size, more preferably from about .5 mm to about 2.5 mm in size and most preferably about 1 mm in size, and are relatively soft and blunt-edged, so that they are advantageous for safe, harmless passage through the vessels of the body.

Another method of creating multiple fracture initiation sites in a biodegradable polymer is to create periodic regions of pre-degraded material along a stent or a structural element of a stent, such as a monofilament. Post-extrusion or molding operations such as localized degradation of molecular weight of crystalline materials may be performed with lasers, focal UV light sources, water or steam hydrolysis, or irradiation. When the material is presented into an environment that provides heat and moisture for hydrolytic polymer degradation, the pre-degraded regions will lose strength and disintegrate sooner than regions of the material that were not pre-degraded. The frequency of occurrence of the pre-degraded regions will affect the size of the fracture pieces from disintegration. A low frequency of pre-degradation regions will result in disintegration into relatively large pieces. A high frequency will result in disintegration into relatively small pieces.

In addition to, or as an alternative to, manipulating the molecular structure, mechanical disintegration and/or fracture sites may be designed into the implant to cause predictable, controlled fracture and/or disintegration. Mechanical disintegration initiation sites may be created in the material or implant, for example, by purposely notching, grooving, indenting, or contouring the surface. Internal mechanical initiation sites may be created by purposely introducing porosity or foreign particles in the solidifying polymer.

Alternatively, unmodified bioabsorbable polymers may be used in the form of thin monofilaments or cable strands to construct the stent. Thinner monofilaments disintegrate into finer particles than the thicker (0.25 mm diameter) monofilaments. Thus, one embodiment of the invention relates to replacing the standard 24 single strands of 0.25 mm diameter bioabsorbable polymer monofilament with 24 paired strands of 0.12 mm diameter monofilament or, alternatively, 24 strands of pre-braided cable each containing two or more monofilaments of very fine diameter, about 0.05 mm or less in diameter. This embodiment of the present invention may also be extrapolated for use in large stents such as 22 mm diameter esophageal or colonic stents where large diameter monofilaments would traditionally be used in the braids. It is beneficial to control the disintegration particle size in these large stents by using multiple, small diameter filaments in their design so that the fragments are be less harmful and more easily passed through the vessel system out of the body.

Additionally, the disintegrating stents of the present invention may be designed so that they are strained by the body to promote disintegration at purposely created weak spots within the material. An example would be to significantly oversize all or portions of a self-expanding stent within a vessel. Prior to implantation the device would be unstrained. After delivery to and release within the target vessel, the stent may be strained, as a result of its larger size relative to the vessel diameter. This strain will facilitate fracture of the stent at the pre-manufactured weak spots after a pre-determined amount of time and the stent will break into small soft particles to be carried away by the vessel contents.

The disintegrating stent of the present invention may be positioned to serve as a bridge to surgery, bridge to radiation, or bridge to onset of drug therapy. The stent may also be used to hold issues in place while healing occurs, for example after traumatic injury or surgery. Stents intended for management of obstructed lumens may be made in this manner where the stent was only needed to be present for couple of weeks to a few months; e.g., for a bridge to adjuvant therapy or surgery.

Disintegrating stents of the present invention may be delivered to the target lumen using a Unistep Plus™ or other catheter type of delivery system. The stents may be implanted as are metal or bioabsorbable Wallstents.

The present invention may be used advantageously in connection with all manner of stents. A preferred embodiment of the invention relates to improved bioabsorbable stents. In particular, all features of the bioabsorbable stents described in U.S. Patent Application No. 08/904,467, filed August 1, 1997, are considered by the inventors to be features of the present invention.

Still other objects and advantages of the present invention and methods of construction of the same will become readily apparent to those skilled in the art from the following detailed description, wherein only the preferred embodiments are shown and described, simply by way of illustration of the best mode contemplated of carrying out the invention. As will be realized, the invention is capable of other and different embodiments and methods of construction, and its several details are capable of modification in various obvious respects, all without departing from the invention. Accordingly, the drawing and description are to be regarded as illustrative in nature, and not as restrictive.

Description of the Drawings

Figure 1a is an isometric view of an example of a braided filament bioabsorbable stent, comprised of 0.25 mm single filament strands, that may be used in connection with the present invention;

Figure 1b' is a simplified representation of a braided tubular stent of the type illustrated in Figure 1a;

Figure 1b shows an alternative braid structure for the braided tubular bioabsorbable stent shown in Figures 1a and 1b';

Figure 1c shows a second alternative braid structure for the braided tubular bioabsorbable stent shown in Figures 1a and 1b' in which the stent is comprised of 0.12 mm paired filament strands;

Figure 1d shows a third alternative braid structure for the braided tubular bioabsorbable stent shown in Figures 1a and 1b' in which the stent is comprised of 0.25 mm (overall) cable strands;

Figure 2 is a partial longitudinal cross-sectional view of the stent shown in Figure 1a;

Figure 3 is a cross-sectional view of one of the filaments of the stent shown in Figure 1a;

Figure 4 is an isometric view of an example of a bioabsorbable stent comprised of a single helical coil of polymer monofilament that may be used in connection with the present invention;

Figure 5 is an isometric view of a rolled film or sheet-type bioabsorbable stent that may be used in connection with the present invention;

Figure 6 is an isometric view of a solid extruded or molded tube-type bioabsorbable stent that may be used in connection with the present invention;

Figure 7 is an isometric view of a knitted or woven polymer filament-type bioabsorbable stent that may be used in connection with the present invention;

Figure 8 is a representation of a polymer monofilament having bands of crystalline material separated by amorphous material;

Figure 9 is a representation of a polymer monofilament having a center core of more crystalline material and a surface of more amorphous material;

Figure 10 is a representation of a polymer monofilament having a heterogeneous structure of crystalline and amorphous regions randomly dispersed throughout its cross-section;

Figure 11 is a representation of another embodiment of the invention according to which localized pre-degraded regions are created by exposure to heat, light, moisture or radiation;

Figures 12a-12c are representations of further embodiments of the invention according to which surface initiation sites are created, for example, by notching, by grooving, or by indenting of the filament or stent surface;

Figure 13 is a representation of another embodiment of the invention according to which filaments are contoured to provide narrowed sections to facilitate controlled fracture;

Figure 14 is a representation of another embodiment of the invention according to which internal disintegration initiation sites are provided, for example by introducing pores, air pockets or foreign particles into the filament;

Figure 15 is a side view of a delivery device with the stent shown in Figure 1 loaded thereon;

Figure 16 is a detailed view of the portion of the delivery device encircled at "Fig. 16" in Figure 15;

Figure 17 is a detailed view of the portion of the delivery device encircled at "Fig. 17" in Figure 15;

Figures18-21 are partial cross-sectional side views of the distal portion of the delivery device and stent shown in Figure 15 at various stages during a stent deployment operation in a body vessel;

Figure 22 is a side view of a pusher-type delivery device;

Figure 23 is a side view of a second embodiment of a stent in accordance with the present invention;

Figure 24 is an end view of the stent shown in Figure 23.

Detailed Description of the Invention

An implantable prosthesis or stent 10 according to a preferred embodiment of the present invention is illustrated generally in Figures 1a and 2. Figure 4 shows an

alternative embodiment of the invention according to which the stent is comprised of a single helical coil of polymer monofilament. Figure 5 shows an alternative embodiment of the invention according to which the stent is compirised of a rolled film or sheet. Figure 6 shows an alternative embodiment of the invention according to which the stent is comprised of a solid extruded or molded tube. Figure 7 shows an alternative embodiment of the invention according to which the stent is comprised of knitted or woven polymer filaments. Stents of the type illustrated in Figures 4-7 are generally well-known in the art and may be manufactured according to well-known methods. Any of the stents according to the embodiments of Figures 4-7 may be made using bioabsorbable or biostable materials.

Referring again to the preferred embodiment of Figures 1a and 2, stent 10 is a tubular device formed from two sets of oppositely-directed, parallel, spaced-apart and helically wound elongated strands or filaments 12. The stent of Figures 1a and 2 is described in more detail in U.S. Patent Application no. 08/904,967, filed August 1, 1997. In particular, the sets of filaments 12 are interwoven in an over and under braided configuration intersecting at points such as 14 to form an open mesh or weave construction. According to one embodiment of the invention, at least one and preferably all filaments 12 consists of one or more commercially available grades of polylactide, poly-L-lactide (PLLA), poly-D-lactide (PDLA), polyglycolide (PGA), polydioxanone, polycaprolactone, polygluconate, polylactic acid-polyethylene oxide copolymers, modified cellulose, collagen, poly(hydroxybutyrate), polyanhydride, polyphosphoester, poly(amino acids), poly(alpha-hydroxy acid) or related copolymers materials. Methods for fabricating stents 10 are generally known and disclosed, for example, in the Wallsten U.S. Patent 4,655,771 and the Wallsten et al. U.S. Patent 5,061,275.

Stent 10 is shown in its expanded or relaxed state in Figures 1a and 2, i.e., in the configuration it assumes when subject to no external loads or stresses. The filaments 12 are resilient, permitting the radial compression of stent 10 into a reduced-radius, extended-length configuration or state suitable for delivery to the desired placement or treatment site through a body vessel (i.e., transluminally). Stent 10 may also be self-expandable from the compressed state, and axially flexible.

According to one embodiment of the invention, stent 10 may be a radially and axially flexible tubular body having a predetermined diameter that is variable under axial

movement of the ends of the body relative to each other. Stent 10 may be composed of a plurality of individually rigid but flexible and elastic thread elements or filaments 12, each of which may extend in a helix configuration along a longitudinal center line of the body as a common axis. The filaments 12 may define a radially self-expanding body. The body may be provided by a first number of filaments 12 having a common direction of winding but axially displaced relative to each other, and crossing a second number of filaments 12 also axially displaced relative to each other but having an opposite direction of winding.

Other structures and features may be included in the stents of the present invention, for example, stents having features which enhance or cooperate with the tubular and self-expandable structure or which facilitate the implantation of the structure. One example is the inclusion of radiopaque markers on the structure which are used to visualize the position of the stent through fluoroscopy during implantation. Other examples include collapsing threads or other structures to facilitate repositioning of the stent.

In the absence of designed controlled fracture, structural failure of stents can result in the breaking loose of large pieces which may damage tissue and/or lodge in and obstruct the lumen. Thus, the present invention is directed towards the design of stents that disintegrate with planned, controlled fracture into small soft fragments that may be easily carried away by body fluids and eliminated from the body.

Mechanisms for the planned controlled disintegration and/or fracture of stents according to the invention are described in the following examples with reference to Figures 10 through 14.

Example 1

One method of creating multiple fracture initiation sites in a biodegradable polymer is to create a structure having more amorphous and less crystalline regions in the material.

Methods for making polycrystalline monofilaments are generally known. For example, methods for making PLA monofilaments are described in detail in U.S. Patent Application 08/08/904,467, filed August 1, 1997. Generally, PLA monofilaments may be produced by a process involving seven general steps as summarized herein. Methods of making monofilaments from other polycrystalline polymers, including but not limited

to the polymers enumerated hereinabove, are equally well known to those of ordinary skill in the art, and this example is not intended to limit the present invention in any way.

First, a polymer formed of poly-L-lactic acid is brought to an elevated temperature above the melting point, preferably 210°- 230°C. Second, the material is then extended at the elevated temperature into a continuous fiber, by a conventional process, at a rate about of three to four feet per minute. Third, the continuous fiber is then cooled to cause nucleation. The cooling is preferably performed by passing the fiber through a nucleation bath of water. Fourth, the material then passes through a first puller, which runs at about the same speed as the extruder, and places the material under slight tension. Fifth, the fiber is then heated to a temperature between about 60°C and about 90°C (preferably 70°C) as it passes through a heated oven. To perform annealing, the oven can be designed to be quite long and heated near the end, so that the orientation and annealing take place in the same oven. Alternatively, a separate oven can be placed directly after the orientation oven. The annealing step heats the fibers to a range of about 65°C to about 90°C, preferably closer to 90°C. Sixth, while being heated in the orientation oven and the annealing oven, the fiber is drawn between the first puller located before the orientation oven and a second puller located after the annealing oven (if a separate oven). The material is drawn at a draw ratio of between about 5 to about 9, preferably between about 6 and about 8. Draw ratio describes the extension in length resulting from polymer extrusion or drawing. Quantitatively, the drawing ratio is a unitless value equal to the extruded or drawn length divided by the original length. Maintaining tension through the annealing step prevents shrinkage in later use. The second puller, located at the exit of the oven, runs at an increased speed necessary to provide the desired draw ratio. As the fiber exits the oven and passes through the second puller the tension is immediately released before the material cools. Seventh, finally, the fiber is collected onto spools of desired lengths.

Degradation is known to occur faster in amorphous material than in crystalline material. Polycrystalline polymers are generally amorphous because of the material's slow crystallization kinetics. Previously, the goal of the stent engineer was to make the filaments as crystalline as possible. Very slow cooling after drawing of the filament or use of a nucleating agent will cause increased crystallization. Alternatively, the material

can be annealed at temperatures above 60 °C to cause crystallization. However, according to the present invention, a more amorphous filament is desired, characterized by fewer regions of crystalline, oriented regions located among more numerous amorphous regions. Therefore, the amorphous regions act as initiation sites for fracture if the amorphous area is large enough to form a fissure or crack that can propagate through the section thickness of the material or to another fissure or crack.

The more amorphous structure can be created, for example, by controlling the solidification cooling rate of the polymer. Fast cooling prevents nucleation and growth of crystallites and slow cooling promotes crystallization. Polymer extrudate that is cooled quickly will have less crystallinity than a more slowly cooled extrudate. If the monofilament extrudate can be cooled along the length with alternating fast and slow cooling rates, a banded structure will form, Figure 8. One method of doing this is pulsing the pull rate of the extrudate filament through the cooling bath after it exits the spinnerette. Another method is to use cooling jet nozzles directed at the extrudate and alternately pulse colder and warmer water as the material is being pulled past the nozzle. If the section size of the extrudate is large enough, a gradient of crystallinity can be created from surface to center. The center of the thickness will cool more slowly than the surface because of heat transfer kinetics. If the temperature gradient is sufficiently large, the center will be more crystalline than the material near the surface, Figure 9. In use, the material near the surface will degrade more rapidly than the center, because it has more amorphous regions. Disintegration will occur by delamination of material near the surface from the more crystalline core. The remaining intact material in the core of the structural element will have reduced section size relative to the initial element (prior to degradation and disintegration of the surface), and in the end, it would disintegrate into smaller pieces than if the entire structural element were to have fractured at once. Uncontrolled crystallization occurs by nucleation and growth of crystallites in the cooling extrudate resulting in a structure comprising pockets of crystalline regions randomly dispersed in amorphous regions, Figure 10. The difference between controlled and uncontrolled heterogeneity is illustrated in Figures 8-10.

The concentration and morphology of the fast-degrading amorphous regions directly relate to the disintegration product size. Accordingly, persons of ordinary skill in the art can easily vary the rate of cooling to adjust the relative proportion of amorphous

regions and crystallized regions to achieve the desired disintegration product size, preferably small enough to easily be carried away by body fluids and eliminated.

Example 2

Mechanical properties generally increase with increasing molecular weight. For instance, the strength and modulus of polycrystalline polymers generally increase with increasing molecular weight. Conversely, degradation time generally decreases with decreasing initial molecular weight (i.e., a stent made of a low molecular weight polymer is bioabsorbed more quickly than a stent made of a high molecular weight polymer). Moreover, the molecular weight and mechanical properties of the material generally decreases as degradation progresses. Accordingly, in addition to, or as an alternative to, the creation of a heterogeous molecular structure to promote controlled disintegration and fracture, the stent material may be subjected to post-extrusion or molding operations to create pre-selected "weak spots," localized pre-degradation of the molecular weight of the crystalline structure of the polymer. One method of creating pre-degraded regions in a monofilament is to mask some portion of the surface and expose the bare surface areas to treatments known to cause degradation in bioabsorbable polymers such as heat, light or other UV radiation, and heated water or steam, Figure 11. According to this embodiment of the invention, a long length of braided bioabsorbable polymer monofilament stent is manufactured, and its surface is then masked with removable strips that are wrapped around the circumference of the stent. The stent is then passed through treatment nozzles to project heat, UV radiation, or heated water onto the surface. The rate of movement of the stent through the nozzles is set to allow sufficient residence time within the treatment medium to cause degradation of the bare polymer or repeated passes can be made. The maskant is then removed and the stent is cut into pieces of the finished design length and packaged for sterilization and subsequent medical use. Examples of treatment media would include quartz lamps or lasers to create heat, ultraviolet lamps to project UV radiation, and steam to supply heated moisture.

Example 3

In addition to manipulating the molecular structure during or after extrusion, mechanical features such as stress concentrations, fissures, notches grooves, indentations or surface contours may be designed into the implant to cause predictable, controlled fracture and/or disintegration. Figures 12a-c and 13 illustrate types of mechanical features

may be introduced into the surfaces of stent materials to facilitate planned and controlled fracture.

Such periodic fracture initiation sites are designed such that they are not deleterious enough to initiate fracture in full-strength material. However, when degradation occurs and the material loses strength, the stress concentrations or fissures become more significant relative to the strength of the material and serve as points of weakness in the device in order to facilitate disintegration. The methods of making the features include lathe turning, milling, drilling, die-forming, laser curing, and chemical etching. Die chatter marks during polymer extrusion may also be advantageous for creating surface crack initiation sites. Usually die chatter is considered an undesirable aesthetic and structural feature. Larger, more pronounced surface features for initiating fracture upon degradation may be produced by localized stretching or die-forming to create a contoured profile in the filament. The contours may be transitions from full thickness to reduced thickness sections. The reduced thickness sections would have lower break loads and would preferentially fracture during degradation.

Example 4

According to yet another embodiment of the invention multiple initiation sites for fracture of the device into small pieces upon disintegration are created by internal porosity or discontinuities in the material. Internal porosity can be created, for example, by purposely causing gas entrapment within the polymer melt during melt extrusion. This may be done, for example, by purging the extrusion chamber with gas or by not applying sufficient vacuum to the chamber to evacuate all of the gas from the liquid polymer. Internal discontinuities may be created, for example, by blending the polymer resin with foreign particles. The particles may be biocompatible and may be dissolvable by the bodily fluids in which the device is to be implanted. If the device is to be implanted in the digestive system, the particles need not be bioabsorbable. They need only be small enough to not cause obstruction of the digestive tract. Examples of biocompatible particles that may be blended with the polymer resin include polymer microspheres (the polymer may be of the same material as the device and be hollow and/or they may be made from a different polymer material) and organic radiopaque agents such as barium sulfate and bismuth trioxide.

Example 5

According to an alternative embodiment of the invention, the filament structure of the stent may be modified to facilitate planned and controlled disintegration. According to this embodiment, optionally unmodified bioabsorbable polymers may be used in the form of thin monofilaments or cable strands to construct the stent. For example, instead of braiding a tubular stent from, for example, 24 single strands of 0.25 mm diameter bioabsorbable polymer monofilament as in Fig. 1b and described in U.S. Patent Aplication No. 08/904,467, the stent may be made from 24 paired strands of 0.12 mm diameter monofilament, Fig. 1c, or 24 strands of pre-braided cable each containing two or more monofilaments of very fine diameter, about 0.05 mm or less in diameter, Fig. 1d. According to this embodiment, the thinner monofilaments disintegrate into finer particles than the thicker (0.25 mm diameter) monofilament. Accordingly, if the filaments are otherwise unmodified, the entire stent disintegrates generally uniformly, but much more quickly and into smaller particle size as compared to stents made with filaments of larger diameter. Of course, if the smaller filaments of this embodiments are manufactured or treated according to any one or more of examples 1-3 herein, the disintegration and/or fracture will proceed accordingly.

Figures 15-17 are illustrations of a coaxial inner/outer tube catheter delivery device 20 for delivering stent 10 to a treatment site in a body vessel.

As shown, stent 10 may be carried by the distal portion of delivery device 20, and is placed on the delivery device in a radially contracted or compressed state. The proximal portion of delivery device 20 generally remains outside of the body for manipulation by the operator.

The manner by which delivery device 20 is operated to deliver stent 10 to a treatment site in a body vessel or lumen including curved sections is illustrated in Figures 18-21. As shown, stent 10 is placed in a radially compressed state in a surrounding relationship to the outer distal end of inner tube 30. Stent 10 is constrained on inner tube 30 by the double-walled section of hose 55. It is important that stent 10 not be confined too tightly on inner tube 30. Hose 55 should apply just enough force to stent 10 to hold stent 10 in place. The double-walled section of hose 55 can be removed from around stent 10 by pulling valve body 40 and proximal tube 50 in a proximal direction. The

double-walled section "rolls" off stent 10. No sliding movements take place between stent 10 and inner wall 56 which contacts stent 10. Along with the movement of the double-walled section in a proximal direction, the distal end of stent 10 will be exposed in a radial direction to engagement against the wall of the body vessel. As the double-walled section of hose 55 continues moving proximally, more of stent 10 expands in a radial direction until the entire length of stent 10 is exposed and engages the wall of a body vessel.

Lumen 35 is used to enable delivery device 20 to follow a guide wire (not shown) previously inserted percutaneously into the body vessel. The lumen of inner tube 30 can also be used to introduce a contrast fluid to the area around the distal end of delivery device 20 so the position of delivery device 20 can be detected (e.g., through the use fluoroscopy or X-ray techniques).

The stents of the present invention may be delivered by alternative methods or using alternative devices. For instance, the device described in Heyn et al. U.S. Patent No. 5,201,757 may be utilized.

According to another embodiment of the present invention, illustrated in Figures 23 and 24, one end of the stent may be tapered. According to this embodiment, stent 110 is similar to stent 10 described above in that it is a tubular device formed from two sets of oppositely-directed, parallel, spaced-apart and helically wound elongated strands or filaments 112. The sets of filaments 112 are interwoven in an over and under braided configuration intersecting at points such as 114 to form an open mesh or weave construction. One end 116 of stent 110 is tapered and has a diameter which decreases from the diameter of the other portions of the stent to a reduced diameter. Stent 110 can be otherwise identical in structure and fabricated from the same PLLA or absorbable polymer materials as stent 10 described above. Stent 110 can be applied (in the manner of stent 10 described above) to a desired location within a vessel, for example, Vena Cava Inferior, for the purpose of preventing lung emboly. When used in this application, stent 110 can be inserted into Vena Cava with a high degree of precision and functions as a filter.

Although the present invention has been described with reference to preferred embodiments, those skilled in the art will recognize that changes can be made in form and detail without departing from the spirit and scope of the invention.

It will be evident from considerations of the foregoing that the devices of the present invention may be constructed using a number of methods and materials, in a wide variety of sizes and styles for the greater efficiency and convenience of a user.

The present invention relates to improved bioabsorbable stents. In particular, all features of the bioabsorbable stents described in U.S. Patent Application No. 08/904,467, filed August 1, 1997, are considered by the inventors to be features of the present invention.

A bioabsorbable stent that may advantageously be used in conjunction with the present invention is disclosed in J. Stinson's United States Patent Application entitled "Bioabsorbable Self Expanding Stent", Serial No.08/904,467, filed August 7, 1997, and commonly assigned to the assignee of this application.

Another bioabsorbable stent that may advantageously be used in conjunction with the present invention is disclosed in J. Stinson's United States Patent No. 5,980,564 entitled "Bioabsorbable Implantable Endoprosthesis With Reservoir And Method Of Using Same", and commonly assigned to the assignee of this application.

Another bioabsorbable marker that may advantageously be used in conjunction with the present invention is disclosed in J. Stinson's and Claude Clerc's United States Patent Application entitled "Radiopaque Markers And Methods Of Using Same", Serial No. 08/905,821, filed August 1, 1997, and commonly assigned to the assignee of this application.

Another bioabsorbable marker that may advantageously be used in conjunction with the present invention is disclosed in J. Stinson's United States Patent Application entitled "Bioabsorbable Marker Having Radiopaque Constituents And Method Of Using Same", Serial No. 08/904,951, filed August 1, 1997, and commonly assigned to the assignee of this application.

The above described embodiments of the invention are merely descriptive of its principles and are not to be considered limiting. Further modifications of the invention herein disclosed will occur to those skilled in the respective arts and all such modifications are deemed to be within the scope of the invention as defined by the following claims.

I claim:

1. A temporary implantable endoprosthesis comprising:

a tubular, radially compressible and axially flexible structure having one or more controlled fracture initiation sites.

2. A temporary implantable endoprosthesis according to claim 1 that is radially self-expandable.

3. A temporary implantable endoprosthesis according to claim 1 selected from the group consisting of braided stents, helical coil stents, rolled sheet stents, solid extruded or molded tube stents and knitted or woven stents.

4. A temporary implantable endoprosthesis according to claim 1 wherein said endoprosthesis is bioaborbable.

5. A temporary implantable endoprosthesis according to claim 1 comprising: crystallized regions and amorphous regions, wherein said amorphous regions degrade more quickly than said crystallized regions, and wherein said crystallized regions have a shape and dimension to permit their elimination from of the body upon the disintegration of said amorphous regions.

6. A temporary implantable endoprosthesis according to claim 1 comprising non-degraded regions and pre-degraded regions.

7. A temporary implantable endoprosthesis according to claim 6 wherein said non-degraded regions have a shape and dimension to permit their elimination from the body upon the disintegration of said pre-degraded regions.

8. A temporary implantable endoprosthesis according to claim 5 wherein said pre-degraded regions are selected from the group consisting of heat-degraded regions, light-degraded regions, moisture-degraded regions or combinations thereof.

9. A temporary implantable endoprosthesis according to claim 1 wherein said controlled fracture initiation sites are located to facilitate planned fracture of said structure after a pre-determined period into fracture products having a shape and dimension to permit their elimination from the body.

10. A temporary implantable endoprosthesis according to claim 1 wherein said controlled fracture initiation sites are surface features.

11. A temporary implantable endoprosthesis according to claim 10 wherein said surface features are selected from the group consisting of notches, grooves, indents, pores, contours and combinations thereof.

12. A temporary implantable endoprosthesis according to claim 1 wherein said controlled fracture initiation sites are internal features.

13. A temporary implantable endoprosthesis according to claim 12 wherein said internal features are selected from the group consisting of air pockets, foreign particles and combinations thereof.

14. A method of using an implantable endoprosthesis comprising the steps of:

providing a tubular, radially compressible and axially flexible structure having a first diameter and one or more controlled fracture initiation sites;

disposing the structure into a delivery system at a second diameter smaller than the first diameter;

inserting the delivery system and endoprosthesis in a body lumen; and

deploying the endoprosthesis from the delivery system into the body lumen to a third diameter smaller than the first.

15. A method of using an implantable endoprosthesis according to claim 14 wherein said tubular, radially compressible and axially flexible structure is radially self-expandable, comprising the additional step of allowing the endoprosthesis to self expand in the body lumen to a fourth diameter greater than the third diameter.

16. A method of using an implantable endoprosthesis according to claim 14, comprising the additional step of balloon expanding said tubular, radially compressible and axially flexible structure in the body lumen to a fourth diameter greater than the third diameter.

17. A method for treating a site within a vessel of a patient, including:

providing a biocompatible medical device comprised of a tubular, radially compressible and axially flexible structure having a first diameter and one or more controlled fracture initiation sites;

providing a delivery system with the medical device positioned on a portion of the delivery system in the compressed stated at a second diameter smaller than the first diameter;

inserting the portion of the delivery system with the medical device into the patient's vessel at a location spaced from the treatment site, and manipulating the delivery system to advance the medical device through the vessel, to the treatment site;

deploying the medical device from the delivery system, the medical device being deployed at a third diameter smaller than the original free diameter; and

removing the delivery system from the patient with the medical device remaining in and supporting the vessel.

18. A bioabsorbable implantable device made from the process comprising:

providing a plurality of elongate filaments comprising a polymer selected from the group consisting of PLLA, PDLA, PGA, and combinations thereof;

braiding the filaments on a first mandrel of from about 3 mm to about 30 mm diameter at a braid angle of from about 120 degrees to about 150 degrees to form a tubular, radially compressible and axially flexible device, the device having a first diameter of from about 2 mm to about 10 mm larger than the final implanted device diameter; and

annealing the device on a second mandrel at a temperature between about the polymer glass-transition temperature and the melting temperature for a time period

between about 5 and about 120 minutes, the second mandrel having a second diameter smaller than the first diameter.

19. A bioabsorbable implantable device according to claim 18, wherein at least one of said elongate filaments comprises at least 60% amorphous regions.

20. A bioabsorbable implantable device according to claim 18, wherein at least one of said elongate filaments comprises at least 70% amorphous regions.

21. A bioabsorbable implantable device according to claim 18, wherein at least one of said elongate filaments comprise at least 75% amorphous regions.

22. A bioabsorbable implantable device according to claim 18, wherein at least one of said elongate filaments comprise at least 75% amorphous regions.

23. A bioabsorbable implantable device according to claim 18, wherein said process includes the further step of pre-degrading portions of annealed device to create controlled fracture initiation sites.

24. A bioabsorbable implantable device according to claim 18, wherein said process includes the further step of scoring the annealed device to create controlled fracture initiation sites.

25. A bioabsorbable implantable device according to claim 18, wherein said process includes the step of scoring at least one of said elongate filaments to create controlled fracture initiation sites prior to said braiding step.

26. A bioabsorbable implantable device according to claim 18, wherein at least one of said elongate filaments is contoured.

27. A bioabsorbable implantable device according to claim 18, wherein said process includes the steps of adding foreign particles to a polymer melt comprising a

polymer selected from the group consisting of PLLA, PDLA, PGA and combinations thereof, to create controlled fracture initiation sites in at least one of said elongate filaments; extruding said polymer melt into an elongate filament, cooling said elongate filament and annealing said elongate filament, prior to said braiding step.

28. A method of manufacturing a stent comprising:

providing from about 10 to about 30 filaments consisting essentially of poly (alpha-hydroxy acid), the filaments having an average diameter from about 0.15 mm to about 0.60 mm; braiding the filaments at a braid angle of from about 120 degrees to about 150 degrees on a braid mandrel of from about 3 mm to about 30 mm diameter;

removing the braid from the braid mandrel;

disposing the braid on an annealing mandrel having an outer diameter of from about 0.2 mm to about 10 mm smaller than the braid mandrel diameter;

annealing the braid at a temperature between about the polymer glass transition temperature and the melting temperature for a time period between about 5 and about 120 minutes; and

allowing the stent to cool.

29. A method according to claim 28, wherein at least one of said filaments comprises at least 60% amorphous regions.

30. A method according to claim 28, wherein at least one of said filaments comprises at least 70% amorphous regions.

31. A method according to claim 28, wherein at least one of said filaments comprises at least 75% amorphous regions.

32. A method according to claim 28, wherein at least one of said filaments comprises around 80% amorphous regions.

33. A method according to claim 28, including the further step of pre-degrading portions of said stent to create controlled fracture initiation sites.

34. A method according to claim 28, including the further step of scoring said stent to create controlled fracture initiation sites.

35. A method according to claim 28 including the further step of scoring at least one of said filaments to create controlled fracture initiation sites prior to said braiding step.

36. A method according to claim 28, wherein at least one of said filaments is contoured.

37. A bioabsorbable implantable device according to claim 28, wherein said process includes the steps of adding foreign particles to a polymer melt comprising a polymer consisting essentially of poly (alpha-hydroxy acid) to create controlled fracture initiation sites in at least one of said filaments; extruding said polymer melt into a filament, cooling said filament and annealing said filament, prior to said braiding step.

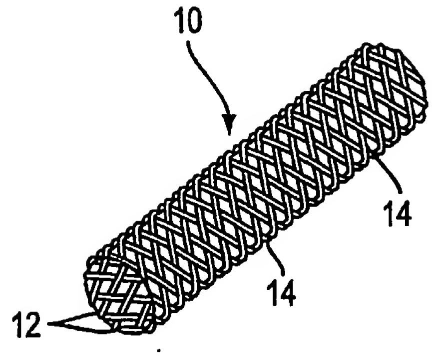

FIG. 1

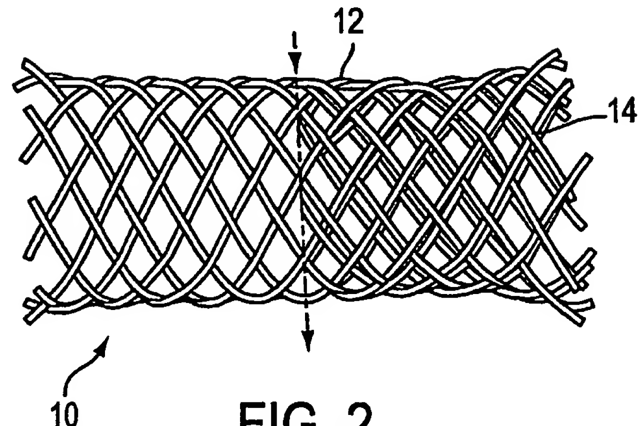

FIG. 2

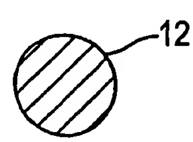

FIG. 3

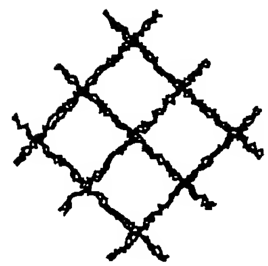

FIG. 1d

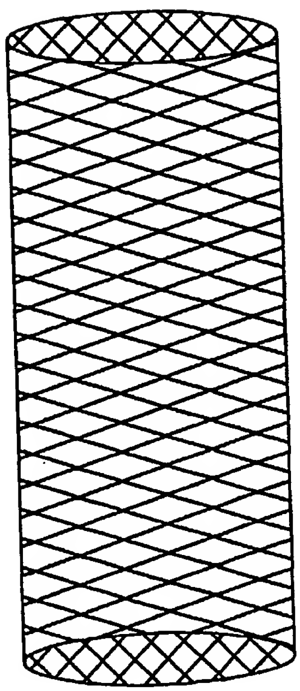

FIG. 1b'

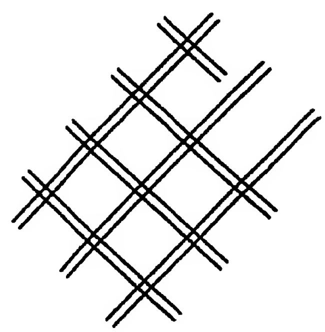

FIG. 1c

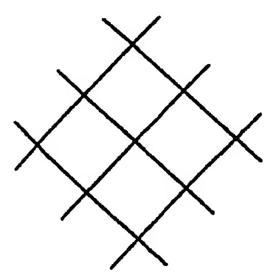

FIG. 1b

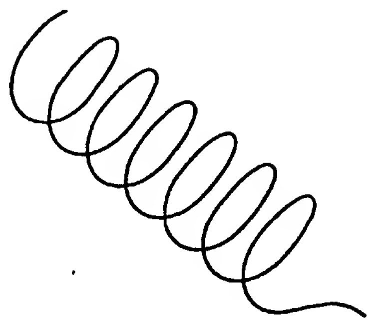

FIG. 4

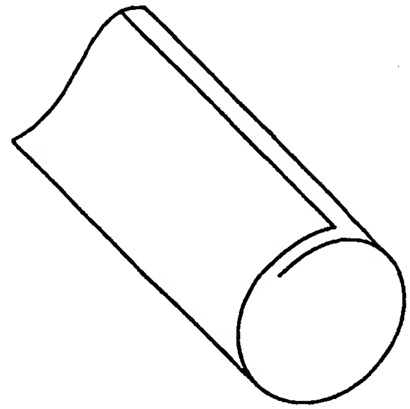

FIG. 5

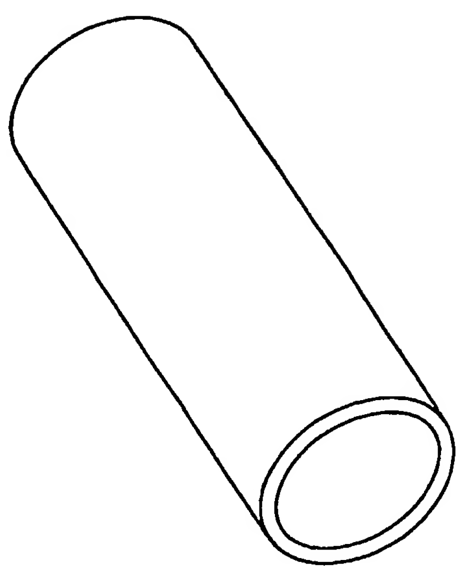

FIG. 6

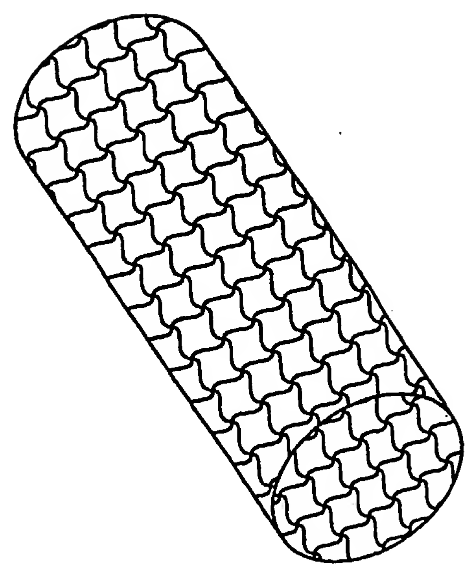

FIG. 7

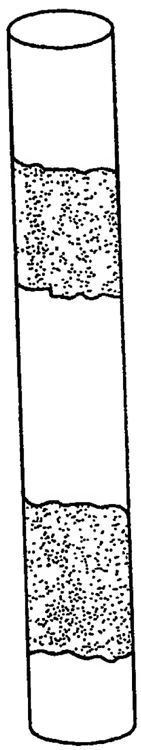

FIG. 8

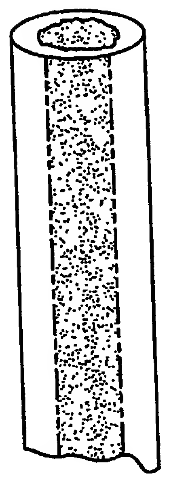

FIG. 9

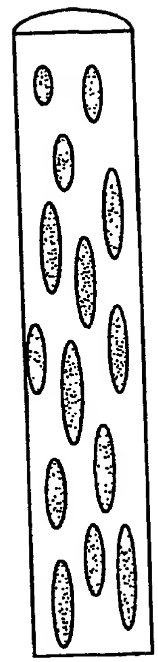

FIG. 10

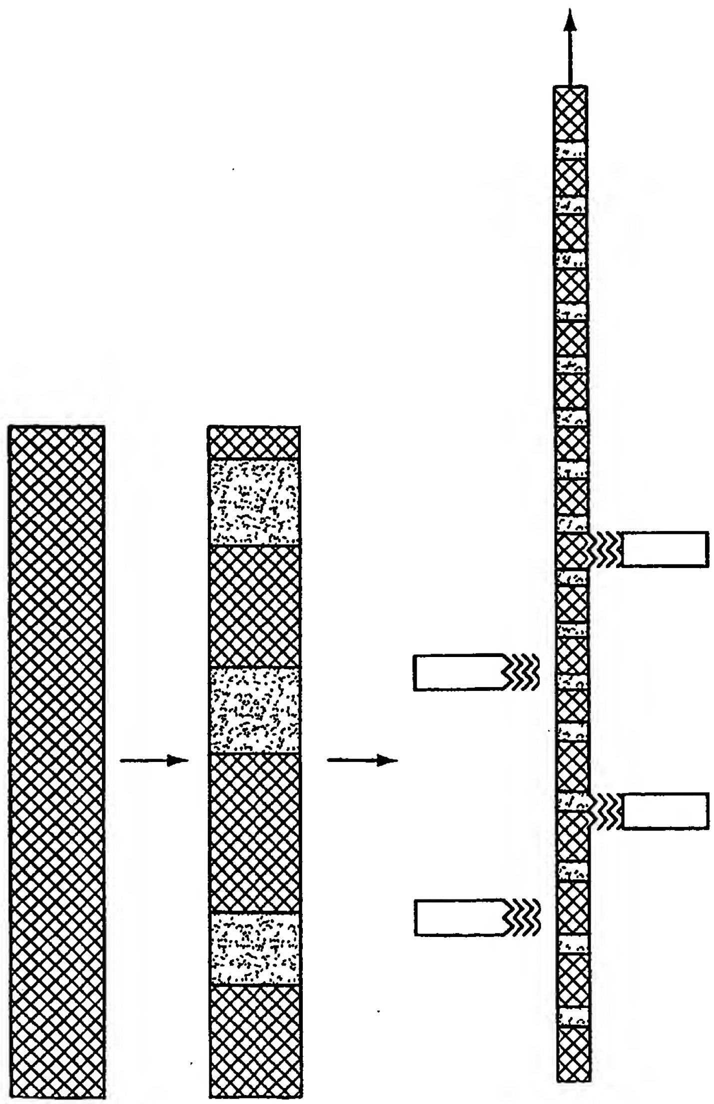

FIG. 11

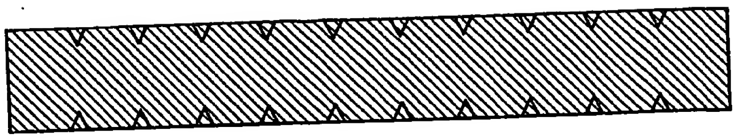

FIG. 12a

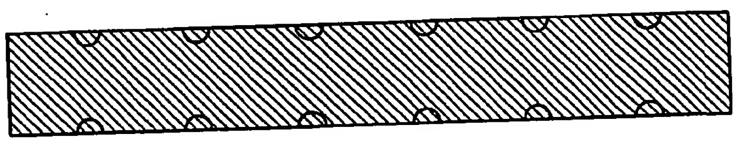

FIG. 12b

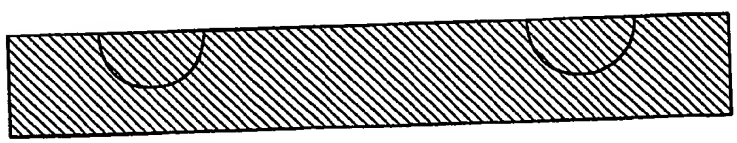

FIG. 12c

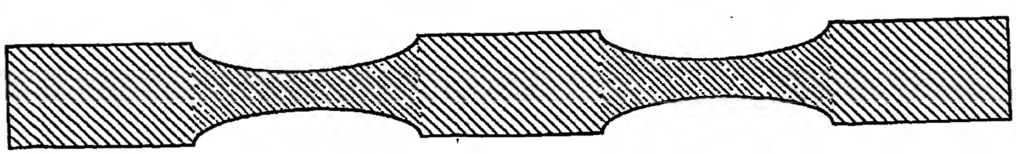

FIG. 13

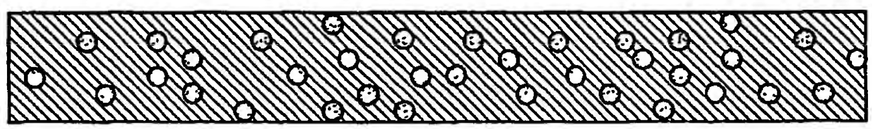

FIG. 14

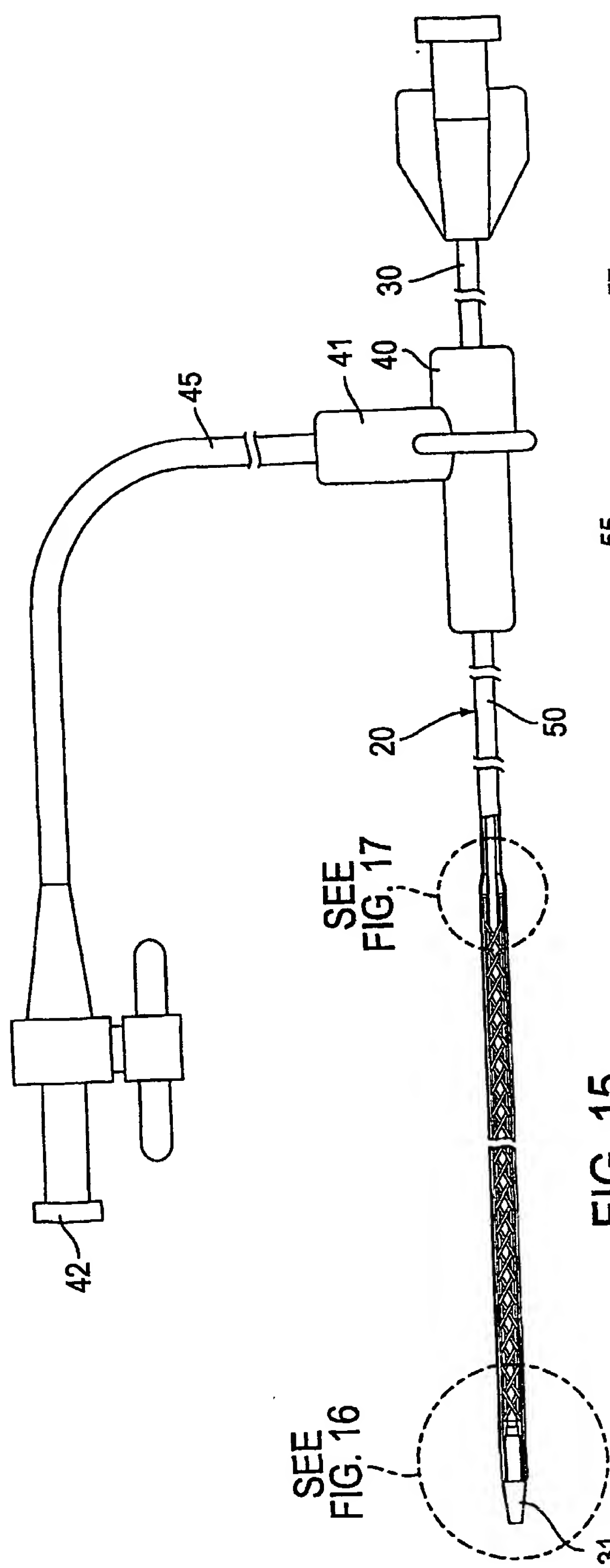

FIG. 15

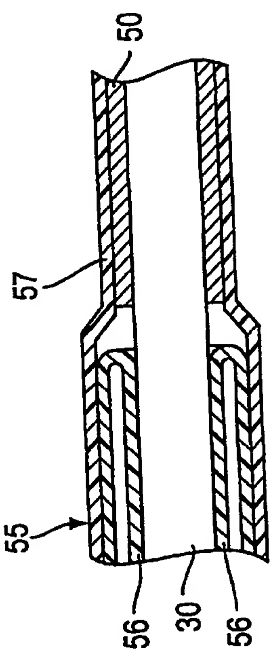

FIG. 17

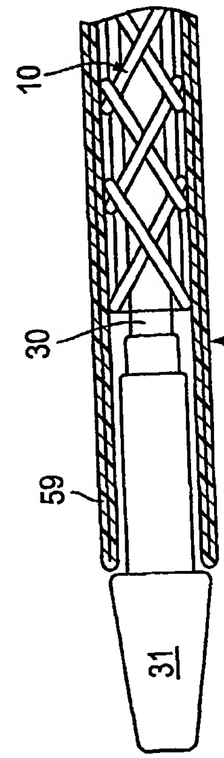

FIG. 16

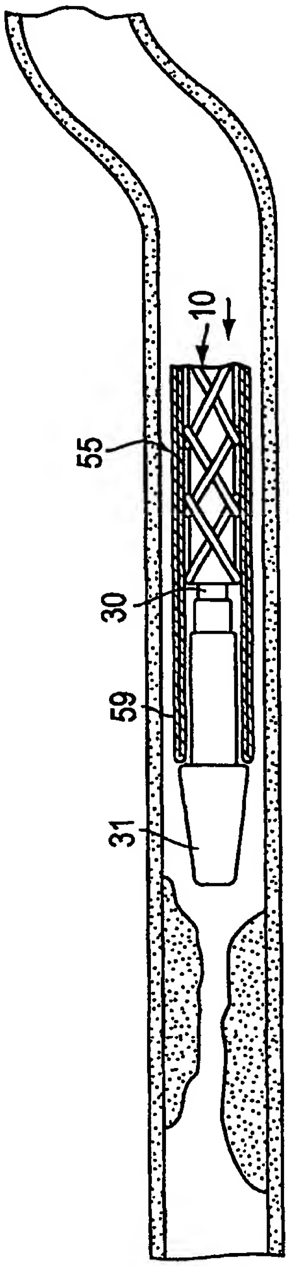

FIG. 18

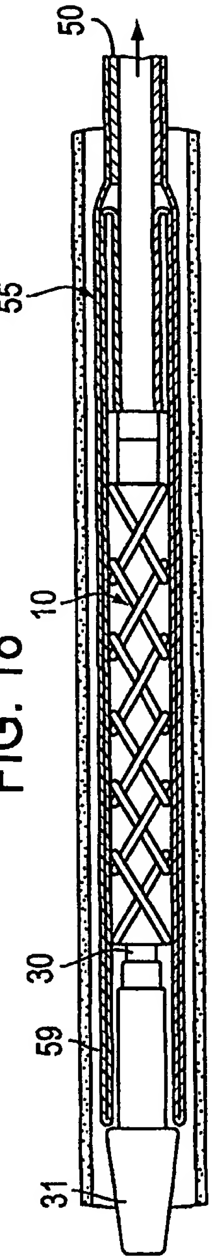

FIG. 19

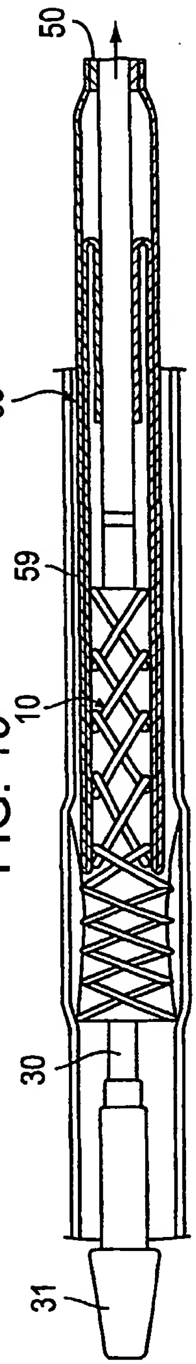

FIG. 20

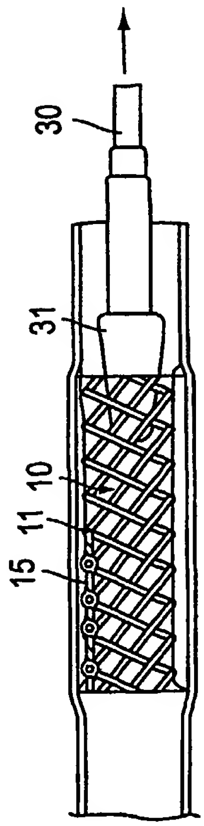

FIG. 21

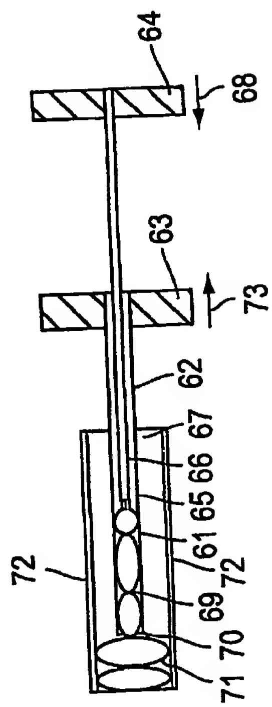

FIG. 22

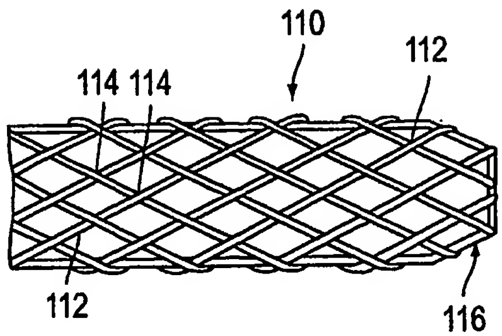

FIG. 23

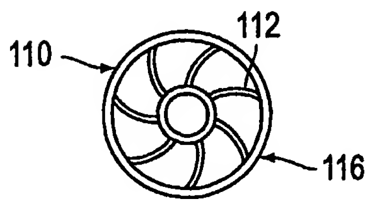

FIG. 24

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/40940

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61F 2/06
US CL :623/1.15
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 623/1.15, 1.38

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,985,307 A (HANSON ET AL.) 16 NOVEMBER 1999, SEE COL. 16, LINE 59 TO COL. 17, LINE 14	1-17
X	US 5,628,787 A (MAYER) 13 MAY 1997, SEE ENTIRE DOCUMENT.	18-37
A	US 6,015,422 A (KERR) 18 JANUARY 2000, SEE COL. 2, LINE 4 TO COL. 3, LINE 8.	1-17

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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